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Progress over the last year on the development of multineuronal recording systems has been significant. Since this was one of the main objectives of the consortium of three laboratories it has been a principle focus of the past years research efforts. This phase is near completion and currently being implemented in several research projects. Consequently most of the research effort in the past year has been directed toward these technological accomplishments. However in addition to the strides made in bringing the multineurone and multi-tasking computer systems to completion, several studies which were in preliminary stages at the time of submission are now near completion and are being prepared for publication. Specifically, these include the signal detection task and the DMTS task in which complex neurophysiological analyses have revealed striking new relationships to sensory processing strategies in the hippocampus and cortex. The accompanying report summarizes these and other accomplishments in the first year of the award.

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Multiple Neuron Recording in the Hippocampus of Freely Moving Animals

Progress Report for AFOSR-90-0092

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Progress Report

Summary

Progress over the last year on the development of multineuronal recording systems has been significant. Since this was one of the main objectives of the consortium of three laboratories it has been a principle focus of the past years research efforts. This phase is near completion and currently being implemented in several research projects. Consequently most of the research effort in the past year has been directed toward these technological accomplishments. However in addition to the strides made in bringing the multineurone and multi-tasking computer systems to completion, several studies which were in preliminary stages at the time of submission are now near completion and are being prepared for publication. Specifically, these include the signal detection task and the DMTS task in which complex neurophysiological analyses have revealed striking new relationships to sensory processing strategies in the hippocampus and cortex. The following report will summarize these and other accomplishments in the first year of the award.

Research Objectives: Statement of Work

The research objectives of the first year of the award were primarily two major projects: 1) to continue to develop and implement technologies and procedures for multiple neurone recording in hippocampus and related structures, and 2) to complete phase I of the initial research plan in which signal detection and delayed match to sample memory tasks were implemented to determine the nature of sensory processing by the hippocampus and relate structures. Each of these objectives will be dealt with in a separate section below.

Development of Multineurone Recording Technology: In the past year two major accomplishments have been achieved by the consortium of Drs Woodward at Dallas, Chapin at Hanneman and our facility here at BGSM. A major role for this laboratory in this effort was to develop and make operational a multi-tasking version of the unitlab software for the motorola realtime operating system (i.e. the delta system). This has been essentially completed and is now ready for implementation and distribution to the other laboratories. The new software will enable the motorola system to control and collect data from several (up to 8) independent stations (behavioral experimental chambers) at a time. This capability was not included in the old version of the software transposed from the original Data General version of Unitlab. The capacity to record from up to 16 channels of analog and unit data from each of the independent stations makes this an extremely powerful laboratory research package for collecting the necessary volume of physiological data from enough animals to achieve statistical significance by projected power analyses, a problem which has plagued this research field for many years.

The second major technological accomplishment in this time period has been the implementation by all three consortium laboratories of the 32 channel DSP (digital signal processing) neurone recording device, developed in conjunction with Spectrum Scientific in Dallas. Our laboratory is the last of the 3 to receive this device since our function was to bring to fruition the multi-tasking aspect of the software outlined above. We currently are in process of installing the DSP technology and interfacing it with our current recording and

analysis systems. The implementation of this device will constitute the final phase of technological design, fabrication, and testing which has been in process over the last 3-4 years by the three independent laboratories.

Personnel:

Dr. Robert Hampson, Ph.D. Research Assist. Professor BGSM.
Mr. Terrence Bunn, Advanced Systems Programmer

Completion of Signal Detection and DMTS Studies, Phase I: Phase I of the project is nearly accomplished as of the submission of this report. To date this includes the completion of initial data collection in two major studies proposed in the original application: 1) auditory signal detection and 2) delayed match to sample (DMTS) memory task. These results are currently in the final stages of analysis and preparation of publication. A brief summary of the findings from each study will be presented below.

Signal Detection Task: Data collection on the auditory signal detection task in rats has now been completed for hippocampus and cortical evoked potentials. Analyses of the data are currently underway with several sophisticated procedures to determine the complex nature of signal processing interactions between the cortex and the hippocampus. Preliminary analyses indicate that "late" cortical potentials (latency >15 msec) evoked on detect vs nondetect trials defined by behavioral criteria, do not follow the same pattern of variation as potentials recorded from the dentate gyrus as reflective of the input from the entorhinal cortex. These data indicate that the processing of sensory information and the manner in which it effects detection of tone stimuli of different intensities on subsequent trials may be a function of the prior biasing of hippocampal synaptic processes to respond to patterned inputs which have been detected by the sensory cortex. The purpose of these studies is to determine the rule by which these biases emerge in terms of the changes in late sensory evoked cortical potentials which are candidates for modification by hippocampal outputs. We have determined and confirmed in the recent series of studies that under some conditions the hippocampus is a primary determinant of cortical late potential amplitudes (i.e. on nondetect trials) while under other conditions the hippocampal evoked potential modifications follow more precisely the changes in late cortical components (i.e. on detect trials).

Thus the completion of phase I of these studies now allows for the further modification of the signal detection paradigm to include selective information biasing of patterned sensory inputs to allow the determination of the "rules" by which such two-way interactive biases between cortex and hippocampus are produced. This will allow the implementation and adaptation of neural computational and neural network modeling to the predictive scheme for simulation of sensory information processing mechanisms.

Delayed Match to Sample Memory Task: The analysis of single hippocampal neurone activity in the DMTS task has been completed in the last 2 months. The analysis is unique in that a thorough compilation of the data from 75 different and independently verified hippocampal neurones meeting the criteria for complex spike cells have been examined in every phase of the task. Several unforseen outcomes were provided by this

unique analysis strategy which gets at the heart of hippocampal cellular participation in information storage and its role in memory processes.

There are five phases to the DMTS task, sample lever presentation, sample lever response, delay interval, match lever presentation, and match lever response. We have found that identified hippocampal cells have unique response patterns in each of these phases and that different subtypes of hippocampal cells are present which selective respond to one or more of these phases of the task. This insight has allowed us to formulate a preliminary model of hippocampal cell function in the task and to simulate these processes in various neural networks portraying hippocampal circuit interactions.

The simulations will provide the basis for further investigations of hippocampal involvement in memory processes by varying the nature of the DMTS task to exercise the unique properties of hippocampal neurones discovered in phase I. In addition the implementation of the multineurone recording capacity and DSP cell identification procedures will provide the basis for integration of the information obtained in phase I, to understanding of the spatial and temporal distribution of the differential roles of particular subtypes of hippocampal cells in and their relationship to the newly described hippocampal anatomic circuitry disclosed by Amaral and Witter (1989). Phase II of the project will therefore be concerned with 1) application of multineurone recording to the DMTS task, and 2) Refinement and further development of the model of hippocampal cellular involvement in memory and information processing.

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Ms. Katherine Alexander, Research Technician, BGSM
Dr. William Levy Ph.D., Modeling Consultant, Associate Professor, University of Virginia.

Publications and Presentations Relevant to This Grant

Hampson, R.E., Foster, T.C., & Deadwyler, S.A. (1989). Effects of delta-9-tetrahydrocannabinol on sensory evoked potentials in the rat: Principal components analysis and sequential dependency. *J. Pharm. exp. Ther.*, **251**, 870-877.

Deadwyler, S.A., Heyser, C.J., Michaelis, R.C., & Hampson, R.E. (1990). The effects of delta-9-THC on mechanisms of learning and memory. In: *Behavior as an Indicator of Neuropharmacological Events*, NIDA Research Monogr., (L. Erinoff, Ed.) 97, 79-93. 1990.

Hampson, R.E., Foster, T.C., & Deadwyler, S.A. (1990). Principal components analysis of hippocampal evoked potentials in the rat. *Brain Res.* (submitted 1990).

Hampson, R.E., Willis, H.H. III, Breese, C.R., & Deadwyler, S.A. (1989) Tone-evoked potentials indicate differential processing of sensory information in the hippocampus and neocortex. *Soc. Neurosci. Abstr.*, **15**, 81.

Heyser, C.J., Hampson, R.E., & Deadwyler, S.A. (1989) Characteristics of hippocampal complex spike neurons during performance of a delayed match to sample task. Selective influences of delta-9-THC. *Soc. Neurosci. Abstr.*, **15**, 11[illegible].

Deadwyler, S.A., Blalock, E.M., Mu., J., & Hampson, R.E. (1990) Delta-9-tetrahydrocannabinol effects on tone evoked potentials recorded from rat neocortex. *Soc. Neurosci. Abstr.*, **16**, 1101.

Hampson, R.E., Wang, S., Bennett, B.A., Morris, M., & Deadwyler, S.A. (1990) Effects of delta-9-tetrahydrocannabinol on whole-cell ion currents in cultured rat hippocampal neurons. *Soc. Neurosci. Abstr.*, **16**, 1019.